Program/Abstract # 196
BMP-switching regulates lineage specification and migration of neural crest cells
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Cell migration is one of the fundamental events during animal development. In developing embryos, neural crest cells (NCCs) emigrate from the neural tube, migrate over a long distance in the body, and undergo final differentiation at their destinations. To understand how such stepwise morphogenesis is regulated during NCC ontogeny, we focus on one of the NCC-lineages, the sympatho-adrenal progenitor cells (SA cells), which give rise to sympathetic neurons (S-cells) and adrenal medulla cells (A-cells). SA cells initially migrate toward the dorsal aorta (DA), and subsequently become segregated into S cells, which remain around DA, and A-cells, which continue to migrate ventrally to the final location of adrenal gland. We found that SA cells are attracted to DA. The DA produces BMPs, which act on neighboring cells. These cells in turn express soluble factors including the chemokine SDF1, a direct attractant for NCC-early migration. BMP signals are also important at later stages where SA cells are segregated into S- and A-cells. Specifically, the SA cells, which are active for BMP-signal when they arrive at DA, turn off the signal thereafter. Subsequently, A-cells but not S-cells reactivate BMP signals. This A-cell-specific reactivation is critical for these cells to migrate ventrally since blocking the BMP reactivation prevented the migration. In contrast, silenced BMP-signaling in the S-cells is important for remaining around the DA. We propose a model that a switching of BMP signals controls distinct steps of migration and lineage specification of NCCs.

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Program/Abstract # 197
CXCR4 controls ventral migration of sympathetic precursor cells
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The molecular mechanisms that sort migrating neural crest cells (NCCs) along a shared pathway into two functionally discrete structures, the dorsal root ganglia (DRG) and sympathetic ganglia (SG), are unknown. We report here that this patterning is due in part to differential expression of the chemokine receptor, CXCR4. We show that 1) a distinct subset of ventrally-migrating NCCs express CXCR4 and this subset is destined to form the neural core of the sympathetic ganglia and 2) the CXCR4 ligand, SDF-1, is a chemoattractant for NCCs in vivo, and is expressed adjacent to the future SG. Reduction of CXCR4 expression in NCCs disrupts their migration towards the future SG while overexpression of CXCR4 in non-SG destined NCCs induces them to migrate aberrantly towards the SG. These data are the first to demonstrate a major role for chemotaxis in the patterning of trunk NCC migration and demonstrate that the neural crest is composed of molecularly heterogeneous cell populations.

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Program/Abstract # 198
Vascular endothelial growth factor regulates cranial neural crest migration in vivo
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The neural crest is an excellent model to study embryonic cell migration, since cell behaviors can be observed in vivo with advanced optical imaging and molecular intervention. A major question is how molecular signals direct neural crest cell (NCC) migration through multiple microenvironments and into specific targets. Here, we tested the hypothesis that the invasion of cranial NCCs, specifically the rhombomere 4 (r4) migratory stream into branchial arch 2 (ba2), is due to chemoattraction through neuropilin-1–vascular endothelial growth factor (VEGF) interactions. Interestingly, the spatio-temporal expression pattern of VEGF in the ectoderm, directly overlying the r4 migratory pathway, correlated with the NCC migratory front. Expression analysis of the r4 migratory stream showed that r4 NCCs expressed neuropilin-1 and VEGF receptor 2. We also found that cranial NCCs were attracted to ba2 tissue or VEGF sources in vitro. To test the in vivo role of VEGF, we injected soluble VEGF receptor 1 (sVEGFR1) distal to the r4 migratory front, to bind up endogenous VEGF, which leads to NCCs failing to completely invade ba2. Time-lapse imaging revealed that VEGF-soaked beads or VEGF-expressing cells placed adjacent to the r4 migratory stream caused NCCs to divert from stereotypical pathways and move towards an ectopic VEGF source. Our results suggest a model in which NCC entry and invasion of ba2 is dependent on chemoattractive signaling through neuropilin-1–VEGF interactions.

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Program/Abstract # 199
Cell division and cell shape patterns during migration of the embryonic chick neural crest revealed by in vivo time-lapse microscopy
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Neural crest cells (NCCs) actively divide and display unique cell morphologies during migration, yet it is unclear whether there is a pattern to cell divisions and changes in cell shape. To study how changes in cell shape may yield clues to how NCCs acquire and maintain direction, we used 3D confocal microscopy and semi-automated cell shape analysis of fluorescently labeled NCCs within transverse sections at the level of rhombomere 4. We will present measurements of changes in NCC orientation as a function of distance along and to the typical migratory pathway in embryos analyzed 8, 16, and 24 h after electroporation to fluorescently label premigratory NCCs. We also investigated NCC division patterns using BrdU staining and 4D confocal time-lapse imaging of multi-color-labeled embryos. We will present results of the orientation of NCC divisions in relation to the direction of migration and position and timing of cell divisions. Our data reveal differences in NCC morphologies and division patterns depending on cell positions within the migratory stream.

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